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In re Application of: )  
AGOSTON ET AL. ) Group Art No: 1623  
Serial No: 09/939,208 )  
Filed: August 24, 2001 )  
For: ANTIANGIOGENIC AGENTS )

### INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents  
Washington, DC 20231

Sir:

The citation of information on the attached Form PTO/SB/08A, "List of Art Cited by Applicant" is made pursuant to 37 C.F.R. §§ 1.97 and 1.98. A copy of all listed items is enclosed. The citation of this information does not constitute an admission that any of the materials are available as a reference or of priority, or a waiver of any right applicant may have under applicable statutes, Rules of Practice in patent cases, or otherwise.

Related applications are listed on the attached Appendix A for your reference. Applicants respectfully request that the Examiner review the applications listed in Appendix A, initial Appendix A in the appropriate spaces, and return a copy of the initialized Appendix to Applicants.

KILPATRICK STOCKTON LLP  
Suite 2800  
1100 Peachtree Road  
Atlanta, Georgia 30309  
(404) 815-6500  
Our Docket: 05213-0852 (43170-263550)

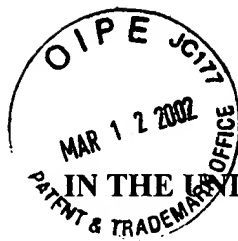
Respectfully submitted,

*Suzanne Seavello Shope*

By: Suzanne Seavello Shope  
Reg. No. 37,933

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, DC, 20231, on this 5<sup>th</sup> day of March 2002.

*Suzanne Seavello Shope*  
Suzanne Seavello Shope - Reg. No. 37,933



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In re Application of:

**Agoston et al.**

Serial No. **09/939,208**

Filed: **August 24, 2001**

For: **ANTIANGIOGENIC AGENTS**

**APPENDIX A**

Assistant Commissioner for Patents  
Washington, D.C. 20231  
Sir:

Applicants respectfully request that the Examiner review the below-listed EntreMed patent applications. Please review and initial each listed application and return a copy of the initialed Appendix A to the Applicants.

The serial numbers of the below-listed U.S. patent applications are listed on this form as provided in MPEP §609(D), rather than a PTO-1449 form, to avoid the serial numbers of the pending U.S. patent applications being published on any patent that may issue from this application. **Applicants do not waive the confidential nature of any of the listed patent applications.**

- \_\_\_\_\_ 1. U.S. Application Serial No. 09/641,327 filed August 18, 2000; Atty. File No. 05213-0730/219693
- \_\_\_\_\_ 2. U.S. Application Serial No. 09/779,331 filed February 8, 2001; Atty. File No. 05213-0731/253406
- \_\_\_\_\_ 3. U.S. Application Serial No. 09/780,650 filed February 12, 2001; Atty. File No. 05213-0493/253692
- \_\_\_\_\_ 4. U.S. Application Serial No. 09/866,279 filed May 25, 2001; Atty. File No. 05213-0412/259097

- \_\_\_\_\_ 5. U.S. Application Serial No. 09/899,702 filed July 5, 2001; Atty. File No. 05213-0910/260981
- \_\_\_\_\_ 6. PCT Application Serial No. PCT/US01/26490 filed August 24, 2001; Atty. File No. 05213-0852WP/263551
- \_\_\_\_\_ 7. U.S. Application Serial No. Not Yet Assigned filed February 15, 2002 by Robert D'Amato entitled "Antiangiogenic Agents and Methods for Treatment of Neovascularization and Related Conditions"; Atty. Docket No. 05213-3000/269288.

Respectfully Submitted,

By: Suzanne Seavello Shope  
Suzanne Seavello Shope  
Reg. No. 37,933

KILPATRICK STOCKTON LLP  
1100 Peachtree Road  
Suite 2800  
Atlanta, Georgia 30309/4530  
(404) 815-6500  
Our Docket: 05213-0852 (43170-263550)

Substitute for Form 1449/A/PTO <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (use as many sheets as necessary)				Complete if Known	
				Application No.	09/939,208
				Filing Date	08/24/2001
				First Named Inventor	Agoston et al.
				Group Art Unit	1623
				Examiner Name	Unassigned
Sheet	1	of	16	Attorney Docket Number	05213-0852 43170-263550

## U.S. PATENT DOCUMENTS

Examiner Initials	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number <sup>2</sup>	Kind Code <sup>3</sup> (if known)			
	1	2,584,271		Huffman	02/05/1952	
	2	2,846,453		Hoehn	08/05/1958	
	3	3,410,879		Smith et al.	11/12/1968	
	4	3,470,218		Farah	09/30/1969	
	5	3,492,321		Crabbe	01/27/1970	
	6	3,496,272		Kruger (Identifier only)	02/17/1970	
	7	3,956,348		Hilscher	05/11/1976	
	8	4,172,132		Draper et al.	10/23/1979	
	9	4,212,864		Tax	07/15/1980	
	10	4,307,086		Tax	12/22/1981	
	11	4,522,758		Ward et al.	06/11/1985	
	12	4,743,597		Javitt et al.	05/10/1988	
	13	4,994,443	B1	Folkman et al.	02/19/1991	
	14	5,001,116		Folkman et al.	03/19/1991	
	15	5,135,919		Folkman et al.	08/04/1992	
	16	5,504,074		D'Amato et al.	04/02/1996	
	17	5,521,168		Clark	05/28/1996	
	18	5,621,124		Seilz et al.	04/15/1997	
	19	5,643,900		Fotsis et al.	07/01/1997	
	20	5,661,143		D'Amato et al.	08/26/1997	
	21	5,892,069		D'Amato et al.	04/06/1999	
	22	6,011,023	B1	Clark et al.	01/04/2000	
	23	6,136,992		Ram et al.	10/24/2000	
	24	6,200,966	B1	Stewart	03/13/2001	

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<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language translation is attached.

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				Filing Date	08/24/2001	
				First Named Inventor	Agoston et al.	
				Group Art Unit	1623	
				Examiner Name	Unassigned	
Sheet	2	of	16	Attorney Docket Number		05213-0852 43170-263550
<b>U.S. PATENT DOCUMENTS</b>						
Examiner Initials	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number <sup>2</sup>	Kind Code <sup>3</sup> (if known)			
	25	6,239,123	B1	Green et al.	05/29/2001	

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Sheet	3	of	16	Attorney Docket Number	05213-0852 43170-263550

## FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No. <sup>1</sup>	Foreign Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>2</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)			
	26	DE	1907330		Sandoz Ltd. (Abstract only)	10/23/1969	
	27	DE	3625315		Schering A.-G (Abstract only)	01/28/1998	
	28	WO	90/15816	A1	The UpJohn Company	12/27/1990	
	29	WO	93/03729		Research Corporation Technologies, Inc.	03/04/1993	
	30	WO	95/04535		The Children's Medical Center Corporation	02/16/1995	
	31	WO	98/40398		Pharm-Eco Laboratories, Inc.	09/17/1998	

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<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language translation is attached.

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Application No.	09/939,208
Filing Date	08/24/2001
First Named Inventor	Agoston et al.
Group Art Unit	1623
Examiner Name	Unassigned
Attorney Docket Number	05213-0852 43170-2638

**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
	32	<b>Author:</b> Title: Lipoiristone/(1-[4-(Dimethylamino)phenyl]-17-hydroxy-17-(3-hydroxy-1-propenyl) estr-4,9-diene-3-one; AK 98734 <b>Publ:</b> Dict. of Drugs (1990), Dict. of Steroids (1991), Dict. of Org. Vol/Iss: Pages: Date: Cmpds (6th Ed) (1996), Dict. of Pharm. Agents (1997)	
	33	<b>Author:</b> Title: (paragraphs 583-584) <b>Publ:</b> The Merck Index 11th Edition Vol/Iss: Pages: 88 Date: 1989	
	34	<b>Author:</b> ADAMS, E.F. et al. Title: Steroidal regulation of oestradiol-17B dehydrogenase activity of the human breast cancer cell line MCF-7 <b>Publ:</b> Journal of Endocrinology Vol/Iss: 188 (1) Pages: 149-154 Date: 07/1988	
	35	<b>Author:</b> AIZU-YOKOTA et al. Title: Natural Estrogens Induce Modulation of Microtubules in Chinese Hamster V79 Cells in Culture <b>Publ:</b> Cancer Research Vol/Iss: 55 Pages: 1863-1868 Date: 05/01/95	
	36	<b>Author:</b> ATTALIA et al. Title: 2-Methoxyestradiol Arrests Cells in Mitosis without Depolarizing Tubulin <b>Publ:</b> Biochemical and Biophysical Research Communications Vol/Iss: 228 Pages: 467-473 Date: 1996	
	37	<b>Author:</b> AYALA et al. Title: The Induction of Accelerated Thymic Programmed Cell Death During Polymicrobial Sepsis: Control by Corticosteroids but not Tumor Necrosis Factor (Abstract only) <b>Publ:</b> Shock Vol/Iss: 3 (4) Pages: 259-267 Date: 04/1995	
	38	<b>Author:</b> BANIK et al. Title: Orally Active Long-Acting Estrogen (3-(2-propynyloxy)-estra-1,3,5,(10)-triene-17. beta.-ol trimethylacetate) (Identifier only) <b>Publ:</b> Steroids Vol/Iss: 16 (3) Pages: 289-296 Date: 1970	

Examiner Signature	Date Considered
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<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language translation is attached.

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (use as many sheets as necessary)				Filing Date	08/24/2001
				First Named Inventor	Agoston et al.
				Group Art Unit	1623
				Examiner Name	Unassigned
Sheet	5	of	16	Attorney Docket Number	05213-0852 43170-263550

**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
	39	<b>Author:</b> BARDON et al. <b>Title:</b> Steroid Receptor-Mediated Cytotoxicity of an Antiestrogen and an Antiprogesterin in Breast Cancer Cells (Abstract only) <b>Publ:</b> <u>Cancer Research</u> <b>Vol/Iss:</b> 47 (5) <b>Pages:</b> 1441-1448 <b>Date:</b> 03/01/87	
	40	<b>Author:</b> BHAT et al. <b>Title:</b> Estradiol-induced Mitotic Inhibition in the Bursa of Fabricius of Male Domestic Duckling <b>Publ:</b> <u>Mikroskopie</u> <b>Vol/Iss:</b> 39 <b>Pages:</b> 113-117 <b>Date:</b> 05/1982	
	41	<b>Author:</b> BLAGOSKLONNY et al. <b>Title:</b> Raf-1/bcl-2 Phosphorylation: A Step from Microtubule Damage to Cell Death <b>Publ:</b> <u>Cancer Research</u> <b>Vol/Iss:</b> 57 <b>Pages:</b> 130-135 <b>Date:</b> 01/01/97	
	42	<b>Author:</b> BLICKENSTAFF et al. <b>Title:</b> Estrogen-Catharanthus (Vinca) Alkaloid Conjugates <b>Publ:</b> <u>Cytotoxic Estrogens in Hormone Receptive Tumors</u> <b>Vol/Iss:</b> <b>Pages:</b> 89-105 <b>Date:</b> 1980	
	43	<b>Author:</b> BOYE et al. <b>Title:</b> 185. Deaminocolchinyll Methyl Ether: Synthesis from 2,3,4,4'-Tetramethoxybiphenyl <b>Publ:</b> <u>Helvetica Chimica Acta</u> <b>Title:</b> -2-carbaldehyde. Comparison of Antitubulin Effects of <b>Vol/Iss:</b> 72 <b>Pages:</b> 1690-1696 <b>Date:</b> 1989	
	44	<b>Author:</b> BRODIE, A.M. <b>Title:</b> Aromatase Inhibitors in the Treatment of Breast Cancer (Abstract only) <b>Publ:</b> <u>Journal of Steroid Biochemistry and Molecular Biology</u> <b>Vol/Iss:</b> 49 (4-6) <b>Pages:</b> 281-287 <b>Date:</b> 06/1994	
	45	<b>Author:</b> BROSENS et al. <b>Title:</b> Comparative Study of the Estrogenic Effect of Ethinylestradiol and Mestranol on the Endometrium <b>Publ:</b> <u>Laboratory for Gynecological Physiopathology</u> <b>Vol/Iss:</b> 14 (6) <b>Pages:</b> 679-685 <b>Date:</b> 12/01/76	

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<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language translation is attached.



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		First Named Inventor	Agoston et al.
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Sheet 6 of 16		Attorney Docket Number	05213-0852 43170-263550

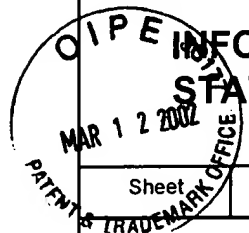
**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

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	46	<b>Author:</b> CASTAGNETTA, L. et al. <b>Title:</b> Simple Approach to Measure Metabolic Pathways of Steroids in Living Cells <b>Publ:</b> <u>Journal of Chromatography</u> <b>Vol/Iss:</b> 572 <b>Pages:</b> 25-39 <b>Date:</b> 12/06/91	
	47	<b>Author:</b> CHASSEROT-GOLAZ et al. <b>Title:</b> Biotransformation of 17.beta.-hydroxy-11.beta.-(4-dimethylaminophenyl) 17.alpha.1-propynyl-estra-4,9-diene-3-one (RU486) in Rat Hepatoma Variants (Identifier only) <b>Publ:</b> <u>Biochemical Pharmacology</u> <b>Vol/Iss:</b> 46 (11) <b>Pages:</b> 2100-2103 <b>Date:</b> 01/01/93	
	48	<b>Author:</b> CHEN et al. <b>Title:</b> A New Synthetic Route to 2- and 4-Methoxyestradiols by Nucleophilic Substitution <b>Publ:</b> <u>Steroids</u> <b>Vol/Iss:</b> 47 (1) <b>Pages:</b> 63-66 <b>Date:</b> 01/1986	
	49	<b>Author:</b> CHEN et al. <b>Title:</b> Synthesis of 11.beta.-(4-dimethylaminophenyl)-17.beta.-hydroxy-17.alpha.-(1-propyl) estra-4, 9-dien-3-one (RU486) (Identifier only) <b>Publ:</b> <u>Nanjing Yaoxueyuan Xuebao</u> <b>Vol/Iss:</b> 17 (4) <b>Pages:</b> 282-285 <b>Date:</b> 1986	
	50	<b>Author:</b> COHEN et al. <b>Title:</b> Novel Total Synthesis of (+)-Estrone 3-Methyl Ether, (+)-13B-Ethyl-3-methoxygona-1,3,5(10-triene-17-one, and (+)-Equilenin 3-Methyl Ether <b>Publ:</b> <u>The Journal of Organic Chemistry</u> <b>Vol/Iss:</b> 6 <b>Pages:</b> 681-685 <b>Date:</b> 03/21/75	
	51	<b>Author:</b> COLLINS et al. <b>Title:</b> The Structure and Function of Estrogens. XI* Synthesis of (+/-)-7(8-11 $\alpha$ ) abeo-Estradiol and its 9,11-Didehydro Derivative <b>Publ:</b> <u>Aust. Journal of Chemistry</u> <b>Vol/Iss:</b> 45 <b>Pages:</b> 71-97 <b>Date:</b> 1992	
	52	<b>Author:</b> CRUM, R. et al. <b>Title:</b> A New Class of Steroids Inhibits Angiogenesis in the Presence of Heparin or a Heparin Fragment <b>Publ:</b> <u>SCIENCE</u> <b>Vol/Iss:</b> 230 <b>Pages:</b> 1375-1378 <b>Date:</b> 12/20/85	

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	53	<b>Author:</b> CUMMINGS et al. <b>Title:</b> Apoptosis <b>Publ:</b> <u>The American Journal of Surgical Pathology</u> <b>Vol/Iss:</b> 21 (1) <b>Pages:</b> 88-101 <b>Date:</b> 1997	
	54	<b>Author:</b> CUSHMAN et al. <b>Title:</b> Synthesis, Antitubulin and Antimitotic Activity, and Cytotoxicity of Analogs of 2-Methoxyestradiol, an Endogenous Mammalian Metabolite of Estradiol that <b>Publ:</b> <u>Journal of Medical Chemistry</u> <b>Vol/Iss:</b> 38 (12) <b>Pages:</b> 2041-2049 <b>Date:</b> 1995	
	55	<b>Author:</b> CUSHMAN et al. <b>Title:</b> Synthesis of Analogs of 2-Methoxyestradiol with Enhanced Inhibitory Effects of Tubulin Polymerization and Cancer Cell Growth <b>Publ:</b> <u>Journal of Medical Chemistry</u> <b>Vol/Iss:</b> 40 (15) <b>Pages:</b> 2323-2334 <b>Date:</b> 1997	
	56	<b>Author:</b> D'AMATO et al. <b>Title:</b> 2-Methoxyestradiol, an Endogenous Mammalian Metabolite, Inhibits Tubulin Polymerization by Interacting at the Colchicine Site <b>Publ:</b> <u>Proceedings of the National Academy of Science USA</u> <b>Vol/Iss:</b> 91 <b>Pages:</b> 3964-3968 <b>Date:</b> 04/1994	
	57	<b>Author:</b> DVIR et al. <b>Title:</b> Thin-layer Chromatography of DANSYL-oestrogens <b>Publ:</b> <u>Journal of Chromatography</u> <b>Vol/Iss:</b> 52 <b>Pages:</b> 505-506 <b>Date:</b> 11/04/70	
	58	<b>Author:</b> EPE et al. <b>Title:</b> Microtubular Proteins as Cellular Targets for Carcinogenic Estrogens and Other Carcinogens <b>Publ:</b> <u>Mechanisms of Chromosome Distribution and Aneuploidy</u> <b>Vol/Iss:</b> <b>Pages:</b> 345-351 <b>Date:</b> 1989	
	59	<b>Author:</b> EVANS et al. <b>Title:</b> A Convergent Total Synthesis of (+)- Colchicine and (+)-Desacetamidoisocolchicine <b>Publ:</b> <u>Journal of the American Chemical Society</u> <b>Vol/Iss:</b> 103 <b>Pages:</b> 5813-5821 <b>Date:</b> 09/23/81	

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				Group Art Unit	1623
				Examiner Name	Unassigned
Sheet 8 of 16	Attorney Docket Number 05213-0852 43170-263550				

**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
	60	<b>Author:</b> FISHMAN, J. <b>Title:</b> Synthesis of 2-Methoxyestrogens <b>Publ:</b> <u>Journal of the American Chemical Society</u> <b>Vol/Iss:</b> 80 <b>Pages:</b> 1213-1216 <b>Date:</b> 03/05/98	
	61	<b>Author:</b> FITZGERALD <b>Title:</b> Molecular Features of Colchicine Associated with Antimitotic Activity and Inhibition of Tubulin Polymerization <b>Publ:</b> <u>Biochemical Pharmacology</u> <b>Vol/Iss:</b> 25 <b>Pages:</b> 1383-1387 <b>Date:</b> 06/15/76	
	62	<b>Author:</b> FOTSIS et al. <b>Title:</b> The Endogenous Oestrogen Metabolite 2-Methoxyoestradiol Inhibits Angiogenesis and Suppresses Tumour Growth <b>Publ:</b> <u>Nature</u> <b>Vol/Iss:</b> 368 <b>Pages:</b> 237-239 <b>Date:</b> 03/17/94	
	63	<b>Author:</b> GETAHUN et al. <b>Title:</b> Synthesis of Alkoxy-Substituted Diaryl Compounds and Correlation of Ring Separation with Inhibition of Tubulin Polymerization: Differential Enhancement of Inhibitory Effects Under Suboptimal Polymerization <b>Publ:</b> <u>Journal of Medical Chemistry</u> <b>Vol/Iss:</b> 35 (6) <b>Pages:</b> 1058-1067 <b>Date:</b> 03/20/92	
	64	<b>Author:</b> GROSS et al. <b>Title:</b> Inhibition of Tumor Growth, Vascularization, and Collagenolysis in the Rabbit Cornea by Medroxyprogesterone <b>Publ:</b> <u>Proceedings of the National Academy of Science USA</u> <b>Vol/Iss:</b> 78 (2) <b>Pages:</b> 1176-1180 <b>Date:</b> 02/1981	
	65	<b>Author:</b> GUANGRONG et al. <b>Title:</b> Effect of Components of Crown Ether Copper(I)Iodide Mixed Catalyst on Nucleophilic Substitution of Bromoestrogen (Abstract No. 195225) <b>Publ:</b> <u>Chemical Abstracts</u> <b>Vol/Iss:</b> 111 (21) <b>Pages:</b> 818, Column 1 <b>Date:</b> 11/20/89	
	66	<b>Author:</b> HALDAR et al. <b>Title:</b> Bc12 is the Guardian of Microtubule Integrity <b>Publ:</b> <u>Cancer Research</u> <b>Vol/Iss:</b> 57 <b>Pages:</b> 229-233 <b>Date:</b> 01/15/97	

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<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language translation is attached.

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				Application No.	09/939,208
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (use as many sheets as necessary)				Filing Date	08/24/2001
				First Named Inventor	Agoston et al.
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Sheet	10	of	16	Attorney Docket Number	05213-0852 43170-263550

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	74	<b>Author:</b> KLAUBER at al. <b>Title:</b> Inhibition of Angiogenesis and Breast Cancer in Mice by the Microtubule Inhibitors 2-Methoxyestradiol and Taxol <b>Publ:</b> <u>Cancer Research</u> <b>Vol/Iss:</b> 57 <b>Pages:</b> 81-86 <b>Date:</b> 01/01/97	
	75	<b>Author:</b> LEBRAS, J. et al. <b>Title:</b> Activation and Regioselective Ortho-Functionalization of the A-Ring of B-Estradiol Promoted by "Cp*Ir": An Efficient Organometallic Procedure for the Synthesis of 2-Methoxyestradiol <b>Publ:</b> <u>Organometallics</u> <b>Vol/Iss:</b> 16 <b>Pages:</b> 1765-1771 <b>Date:</b> 1997	
	76	<b>Author:</b> LIN et al. <b>Title:</b> Interactions of Tubulin with Potent Natural and Synthetic Analogs of the Antimitotic Agent Combretastatin: A Structure-Activity Study <b>Publ:</b> <u>Molecular Pharmacology</u> <b>Vol/Iss:</b> 34 (2) <b>Pages:</b> 200-208 <b>Date:</b> 08/1988	
	77	<b>Author:</b> LINCOLN et al. <b>Title:</b> Conformation of Thiocolchicine and Two B-Ring-Modified Analogues Bound to Tubulin Studied with Optical Spectroscopy <b>Publ:</b> <u>Biochemistry</u> <b>Vol/Iss:</b> 30 (5) <b>Pages:</b> 1179-1187 <b>Date:</b> 02/05/91	
	78	<b>Author:</b> LOTTERING et al. <b>Title:</b> Effects of the 17 $\beta$ -Estradiol Metabolites on Cell Cycle Events in MCF-7 Cells <b>Publ:</b> <u>Cancer Research</u> <b>Vol/Iss:</b> 52 <b>Pages:</b> 5926-5932 <b>Date:</b> 11/01/92	
	79	<b>Author:</b> LOTTERING et al. <b>Title:</b> 17 $\beta$ -Estradiol Metabolites Affect Some Regulators of the MCF-7 Cell Cycle <b>Publ:</b> <u>Cancer Letters</u> <b>Vol/Iss:</b> 110 <b>Pages:</b> 181-186 <b>Date:</b> 1996	
	80	<b>Author:</b> MAYOL et al. <b>Title:</b> Ethynylestradiol-Induced Cell Proliferation in Rat Liver Involvement of Specific Populations of Hepatocytes (Abstract only) <b>Publ:</b> <u>Carcinogenesis</u> <b>Vol/Iss:</b> 12 (12) <b>Pages:</b> 2381-2388 <b>Date:</b> 1992	

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	67	<b>Author:</b> HAMEL et al. <b>Title:</b> Interactions of 2-Methoxyestradiol, an Endogenous Mammalian Metabolite, with Unpolymerized Tubulin and with Tubulin Polymers <b>Publ:</b> <u>Biochemistry</u> <b>Vol/Iss:</b> 35 (4) <b>Pages:</b> 1304-1310 <b>Date:</b> 1996	
	68	<b>Author:</b> HARTLEY-ASP et al. <b>Title:</b> Diethylstilbestrol Induces Metaphase Arrest and Inhibits Microtubule Assembly <b>Publ:</b> <u>Mutation Research</u> <b>Vol/Iss:</b> 143 (4) <b>Pages:</b> 231-235 <b>Date:</b> 08/1985	
	69	<b>Author:</b> HE et al. <b>Title:</b> A Versatile Synthesis of 2-Methoxyestradiol, an Endogenous Metabolite of Estradiol which Inhibits Tubulin Polymerization by Binding to the Colchicine Binding Site <b>Publ:</b> <u>Bioorganic &amp; Medicinal Chemistry Letters</u> <b>Vol/Iss:</b> 4 (14) <b>Pages:</b> 1724-1728 <b>Date:</b> 1994	
	70	<b>Author:</b> HUBER et al. <b>Title:</b> Tubulin Binding of Conformationally Restricted Bis-Aryl Compounds <b>Publ:</b> <u>Bioorganic &amp; Medicinal Chemistry Letters</u> <b>Vol/Iss:</b> 1 (5) <b>Pages:</b> 243-246 <b>Date:</b> 1991	
	71	<b>Author:</b> JOSEFSSON et al. <b>Title:</b> Suppression of Type II Collagen-Induced Arthritis by the Endogenous Estrogen Metabolite 2-Methoxyestradiol <b>Publ:</b> <u>Arthritis &amp; Rheumatism</u> <b>Vol/Iss:</b> 40 (1) <b>Pages:</b> 154-163 <b>Date:</b> 01/1997	
	72	<b>Author:</b> KABARITY et al. <b>Title:</b> Further Investigations on the cytological effects of some contraceptives <b>Publ:</b> <u>Mutation Research</u> <b>Vol/Iss:</b> 135 <b>Pages:</b> 181-188 <b>Date:</b> 1984	
	73	<b>Author:</b> KELLY et al. <b>Title:</b> The Stimulation of Prostaglandin Production by Two Antiprogestosterone Steroids in Human Endometrial Cells (Abstract only) <b>Publ:</b> <u>Journal of Clinical Endocrinology Metabolism</u> <b>Vol/Iss:</b> 62 (6) <b>Pages:</b> 1116-1123 <b>Date:</b> 06/1986	

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Attorney Docket Number	05213-0852 43170-263550				
Sheet	11	of	16		

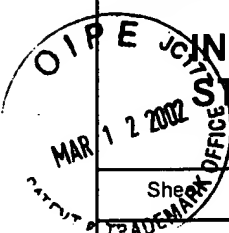
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	81	<b>Author:</b> MEIKRANTZ et al. <b>Title:</b> Apoptosis and the Cell Cycle <b>Publ:</b> <u>Journal of Cellular Biochemistry</u> <b>Vol/Iss:</b> 58 <b>Pages:</b> 160-174 <b>Date:</b> 06/1995	
	82	<b>Author:</b> MILLER et al. <b>Title:</b> Synthesis and Structure-Activity Profiles of A-Homoestranses, the Estratropones <b>Publ:</b> <u>Journal of Medicinal Chemistry</u> <b>Vol/Iss:</b> 40 <b>Pages:</b> 3836-3841 <b>Date:</b> 1997	
	83	<b>Author:</b> MORGAN et al. <b>Title:</b> Calcium and Oestrogen Interactions upon the Rat Thymic Lymphocyte Plasma Membrane <b>Publ:</b> <u>Biochemical and Biophysical Research Communications</u> <b>Vol/Iss:</b> 72 (2) <b>Pages:</b> 663-672 <b>Date:</b> 09/20/76	
	84	<b>Author:</b> MUKHOPADHYAY et al. <b>Title:</b> Induction of Apoptosis in Human Lung Cancer Cells after Wild-Type p53 Activation by Methoxyestradiol <b>Publ:</b> <u>Oncogene</u> <b>Vol/Iss:</b> 14 <b>Pages:</b> 379-384 <b>Date:</b> 1997	
	85	<b>Author:</b> MUKUNDAN et al. <b>Title:</b> Liver Regeneration in Oral Contraceptive Treated Female Rats - Effects of Moderate Malnutrition <b>Publ:</b> <u>Hormone and Metabolic Research</u> <b>Vol/Iss:</b> 16 <b>Pages:</b> 641-645 <b>Date:</b> 12/1984	
	86	<b>Author:</b> NAKAGAWA-YAGI et al. <b>Title:</b> The Endogenous Estrogen Metabolite 2-Methoxyestradiol Induces Apoptotic Neuronal Cell Death <i>In Vitro</i> <b>Publ:</b> <u>Life Sciences</u> <b>Vol/Iss:</b> 58 (17) <b>Pages:</b> 1461-1467 <b>Date:</b> 1996	
	87	<b>Author:</b> NAKAMURA et al. <b>Title:</b> Studies on the Total Synthesis of <i>dl</i> -Colchicine. I. Synthesis of 3-Hydroxy-9, 10, 11-trimethoxy-1,2,3,4,6,7-hexahydro-5H-dibenso[a,c] cycloheptatrien-5-one <b>Publ:</b> <u>Chemical and Pharmaceutical Bulletin</u> <b>Vol/Iss:</b> 10 <b>Pages:</b> 281-290 <b>Date:</b> 1962	

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	95	<b>Author:</b> POLI et al. <b>Title:</b> Tumor Necrosis Factor $\alpha$ Functions in an Autocrine Manner in the Induction of Human Immunodeficiency Virus Expression <b>Publ:</b> Proceedings of the National Academy of Science USA <b>Vol/Iss:</b> 87 <b>Pages:</b> 782-785 <b>Date:</b> 01/1990			
	96	<b>Author:</b> RAVINDRA, R. <b>Title:</b> Effect of Estradiol on the <i>in vitro</i> Assembly of Rat Brain Tubulin <b>Publ:</b> Journal of Indian Institute of Science <b>Vol/Iss:</b> 64 (3) <b>Pages:</b> 27-35 <b>Date:</b> 03/1983			
	97	<b>Author:</b> SAKAKIBARA et al. <b>Title:</b> Effects of Diethylstilbestrol and its Methyl Ethers on Aneuploidy Induction and Microtubule Distribution in Chinese Hamster V79 cells <b>Publ:</b> Mutation Research <b>Vol/Iss:</b> 263 <b>Pages:</b> 269-276 <b>Date:</b> 08/1991			
	98	<b>Author:</b> SATO et al. <b>Title:</b> Effect of Estradiol and Ethynylestradiol on Microtubule Distribution in Chinese Hamster V79 Cells <b>Publ:</b> Chemical and Pharmaceutical Bulletin <b>Vol/Iss:</b> 40 (1) <b>Pages:</b> 182-184 <b>Date:</b> 01/1992			
	99	<b>Author:</b> SATO et al. <b>Title:</b> Disruptive Effect of Diethylstilbestrol on Microtubules <b>Publ:</b> Gann <b>Vol/Iss:</b> 75 <b>Pages:</b> 1046-1048 <b>Date:</b> 12/1984			
	100	<b>Author:</b> SAWADA et al. <b>Title:</b> Colchicine-Like Effect of Diethylstilbestrol (DES) on Mammalian Cells in Vitro <b>Publ:</b> Mutation Research <b>Vol/Iss:</b> 57 <b>Pages:</b> 175-182 <b>Date:</b> 05/1978			
	101	<b>Author:</b> SEEGERs et al. <b>Title:</b> Cyclic-AMP and Cyclic-GMP Production in MCF-7 Cells Exposed to Estradiol-17 Beta, Catecholestrogens and Methoxy-Estrogens in MCF-7 Cells (Meeting Abstract only) <b>Publ:</b> Joint MCI-1st Symposium. Third 1st International Symposium. Biology and Therapy of Breast Cancer <b>Vol/Iss:</b> <b>Pages:</b> <b>Date:</b> 09/25/89			

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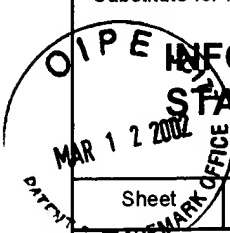
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	88	<b>Author:</b> NAMBARA et al. <b>Title:</b> Studies on Steroid Conjugates. III. New Synthesis of 2-Methoxyestrogens <b>Publ:</b> <u>Chem. Pharm. Bulletin</u> <b>Vol/Iss:</b> 18 (3) <b>Pages:</b> 474-480 <b>Date:</b> 03/1970			
	89	<b>Author:</b> NAPOLITANO et al. <b>Title:</b> 11 Beta-Substituted Estradiol Derivatives. 2. Potential Carbon-11 and Iodine-Labeled Probes for the Estrogen Receptor (Abstract only) <b>Publ:</b> <u>Journal of Medical Chemistry</u> <b>Vol/Iss:</b> 38 (14) <b>Pages:</b> 2774-2779 <b>Date:</b> 07/07/95			
	90	<b>Author:</b> NISHIGAKI et al. <b>Title:</b> Anti-Proliferative Effect of 2-Methoxyestradiol on Cultured Smooth Muscle Cells from Rabbit Aorta <b>Publ:</b> <u>Atherosclerosis</u> <b>Vol/Iss:</b> 113 <b>Pages:</b> 167-170 <b>Date:</b> 1995			
	91	<b>Author:</b> OCHS et al. <b>Title:</b> Effect of Tumor Promoting Contraceptive Steroids on Growth and Drug Metabolizing Enzymes in Rat Liver (Abstract only) <b>Publ:</b> <u>Cancer Research</u> <b>Vol/Iss:</b> 46 (3) <b>Pages:</b> 1224-1232 <b>Date:</b> 1986			
	92	<b>Author:</b> OPPOLZER et al. <b>Title:</b> 177. The Enantioselective Synthesis of (+)-Estradiol from 1,3-Dihydrobenzo[c] thiophene-2,2-dioxide by Successive Thermal SO <sub>2</sub> -Extrusion and Cycloaddition Reactions <b>Publ:</b> <u>Helvetica Chimica Acta</u> <b>Vol/Iss:</b> 63 <b>Pages:</b> 1703-1707 <b>Date:</b> 1980			
	93	<b>Author:</b> PARTHASARATHY et al. <b>Title:</b> Antioxidant: A New Role for RU-486 and Related Compounds (Abstract only) <b>Publ:</b> <u>Journal of Clinical Investigation</u> <b>Vol/Iss:</b> 94 (5) <b>Pages:</b> 1990-1995 <b>Date:</b> 11/1994			
	94	<b>Author:</b> PAULL et al. <b>Title:</b> Identification of Novel Antimitotic Agents Acting at the Tubulin Level by Computer-assisted Evaluation of Differential Cytotoxicity Data <b>Publ:</b> <u>Cancer Research</u> <b>Vol/Iss:</b> 52 <b>Pages:</b> 3892-3900 <b>Date:</b> 07/15/92			

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	102	<b>Author:</b> SEEGERS, J.C. et al. <b>Title:</b> The Cytotoxic Effects of Estradiol-17B, Catecholestradiols and Methoxyestradiols on Dividing MCF-7 and HeLa Cells <b>Publ:</b> <u>Journal of Steroid Biochemistry</u> <b>Vol/Iss:</b> 32 (6) <b>Pages:</b> 797-809 <b>Date:</b> 1989			
	103	<b>Author:</b> SHARP et al. <b>Title:</b> Diethylstilbestrol: the Binding and Effects of Diethylstilboestrol upon the Polymerisation and Depolymerisation of Purified Microtubule Protein in vitro <b>Publ:</b> <u>Carcinogens</u> <b>Vol/Iss:</b> 6 (6) <b>Pages:</b> 865-871 <b>Date:</b> 06/1985			
	104	<b>Author:</b> SPICER et al. <b>Title:</b> Catecholestrogens Inhibit Proliferation and DNA Synthesis of Porcine Granulosa Cells in Vitro: Comparison with Estradiol, 5 $\alpha$ -dihydrotestosterone, Gonadotropins and Catecholamines <b>Publ:</b> <u>Molecular and Cellular Endocrinology</u> <b>Vol/Iss:</b> 64 <b>Pages:</b> 119-126 <b>Date:</b> 1989			
	105	<b>Author:</b> STERNLICHT et al. <b>Title:</b> Colchicine Inhibition of Microtubule Assembly via Copolymer Formation <b>Publ:</b> <u>The Journal of Biological Chemistry</u> <b>Vol/Iss:</b> 254 (20) <b>Pages:</b> 10540-10550 <b>Date:</b> 10/25/79			
	106	<b>Author:</b> SUN et al. <b>Title:</b> Antitumor Agents. 139. Synthesis and Biological Evaluation of Thiocolchicine Analogs 5,6-Dihydro-6(S)-(acyloxy)-and 5,6-Dihydro-6(S)-[(acyloxy)methyl]-1,2,3- <b>Publ:</b> <u>Journal of Medicinal Chemistry</u> <b>Vol/Iss:</b> 36 <b>Pages:</b> 544-551 <b>Date:</b> 03/05/93			
	107	<b>Author:</b> SUNAGAWA et al. <b>Title:</b> Synthesis of Colchicine; Synthesis of dl-'Demethoxydeoxy-hexahydrocolchicine <b>Publ:</b> <u>Chem. Pharm. Bulletin</u> <b>Vol/Iss:</b> 9 <b>Pages:</b> 81-83 <b>Date:</b> 1961			
	108	<b>Author:</b> TERANISHI, M. et al. <b>Title:</b> Methylation of Catechol Estrogen with Diazomethane <b>Publ:</b> <u>Chemical and Pharmaceutical Bulletin</u> <b>Vol/Iss:</b> 31 (9) <b>Pages:</b> 3309-3314 <b>Date:</b> 09/1983			

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				Filing Date	08/24/2001
				First Named Inventor	Agoston et al.
				Group Art Unit	1623
				Examiner Name	Unassigned
Sheets	15	of	16	Attorney Docket Number	05213-0852 43170-263550

**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

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	109	<b>Author:</b> TISHLER et al. <b>Title:</b> Microtubule-Active Drugs Taxol, Vinblastine, and Nocodazole Increase the Levels of Transcriptionally Active p53 <b>Publ:</b> <u>Cancer Research</u> <b>Vol/Iss:</b> 55 <b>Pages:</b> 6021-6025 <b>Date:</b> 12/15/95	
	110	<b>Author:</b> TSUTSUI et al. <b>Title:</b> Comparison of Human Versus Syrian Hamster Cells in Culture for Induction of Mitotic Inhibition, Binucleation and Multinucleation, Following Treatment with Four Aneuploidogens <b>Publ:</b> <u>Toxicology in Vitro</u> <b>Vol/Iss:</b> 4 (1) <b>Pages:</b> 75-84 <b>Date:</b> 1990	
	111	<b>Author:</b> UTNE et al. <b>Title:</b> The Synthesis of 2- and 4-Fluoroestradiol <b>Publ:</b> <u>Journal of Organic Chemistry</u> <b>Vol/Iss:</b> 33 (6) <b>Pages:</b> 2469-2473 <b>Date:</b> 06/1968	
	112	<b>Author:</b> VAN GEERESTEIN et al. <b>Title:</b> Structure of 11.beta.-(4-(dimethylamino)phenyl)-17.beta.-hydroxy-17.alpha.-(2-propenyl) estro-4,9-dien-3-one (Identifier only) <b>Publ:</b> <u>Acta Crystall Ogr., Sect. C: Cryst. Struct. Commun.</u> <b>Vol/Iss:</b> C43 (2) <b>Pages:</b> 319-322 <b>Date:</b> 1987	
	113	<b>Author:</b> VAN TAMELEN et al. <b>Title:</b> The Synthesis of Colchicine <b>Publ:</b> <u>Tetrahedron</u> <b>Vol/Iss:</b> 14 <b>Pages:</b> 8-34 <b>Date:</b> 09/1961	
	114	<b>Author:</b> WANG, Z. et al. <b>Title:</b> An Optimized Synthesis of 2-Methoxyestradiol, a Naturally Occurring Human Metabolite with Anticancer Activity <b>Publ:</b> <u>Synth. Commun.</u> <b>Vol/Iss:</b> 28 (23) <b>Pages:</b> 4431-4437 <b>Date:</b> 1998	
	115	<b>Author:</b> WHEELER et al. <b>Title:</b> Mitotic Inhibition and Aneuploidy Induction by Naturally Occurring and Synthetic Estrogens in Chinese Hamster Cells in Vitro <b>Publ:</b> <u>Mutation Research</u> <b>Vol/Iss:</b> 171 <b>Pages:</b> 31-41 <b>Date:</b> 1986	

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<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language translation is attached.

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	116	<b>Author:</b> WHEELER et al. <b>Title:</b> Mitotic Inhibition and Chromosome Displacement Induced by Estradiol in Chinese Hamsters Cells <b>Publ:</b> Cell Motility and the Cytoskeleton <b>Vol/Iss:</b> 7 (3) <b>Pages:</b> 235-247 <b>Date:</b> 1987			
	117	<b>Author:</b> YUE et al. <b>Title:</b> 2-Methoxyestradiol, an Endogenous Estrogen Metabolite, Induces Apoptosis in Endothelial Cells and Inhibits Angiogenesis: Possible Role for Stress-Activated Protein Kinase Signaling Pathway and Fas Expression <b>Publ:</b> Molecular Pharmacology <b>Vol/Iss:</b> 51 <b>Pages:</b> 951-952 <b>Date:</b> 1997			

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<sup>1</sup>Unique citation designation number. <sup>2</sup>See attached Kinds of U.S. Patent Documents. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language translation is attached.

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